Baskar, P.
09/936921
Searchnotes

(FILE 'HCAPLUS' ENTERED AT 10:51:44 ON 13 NOV 2003)
L8 105 SEA FILE=HCAPLUS ABB=ON PLU=ON WHIPPLE?(1W)(DISEAS? OR DISORDER) OR INTESTIN?(W)(LIPODYSTROPH? OR LIPO DYSTROPH?) OR (TROPHERYM? OR T)(W)WHIPPEL?
L9 59 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN?)
L10 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND VITRO

- key terms

L10 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:905018 HCAPLUS
DOCUMENT NUMBER: 138:105478
TITLE: Dysregulated peripheral and mucosal Th1/Th2 response in **whipple's disease**
AUTHOR(S): Marth, Thomas; Kleen, Nicole; Stallmach, Andreas; Ring, Sabine; Aziz, Sheriff; Schmidt, Carsten; Strober, Warren; Zeitz, Martin; Schneider, Thomas
CORPORATE SOURCE: Internal Medicine II, University of the Saarland, Homburg/Saar, Germany
SOURCE: Gastroenterology (2002), 123(5), 1468-1477
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background & Aims: An impaired monocyte function and impaired interferon (IFN)-γ production has been suggested as a possible pathogenetic factor in **Whipple's disease** (WD) and as a cause for the delayed elimination of Tropheryma whipplei in some patients. Methods: We studied, in a series of 20 WD patients with various degrees of disease activity, cellular immune functions. Results: We found an increase in **vitro** production of interleukin (IL)-4 by peripheral mononuclear blood cells as **determined** by ELISA, but reduced secretion of IFN-γ and IL-2 as compared with age- and sex-matched controls. In addition, we observed a significantly reduced monocyte IL-12 production in response to various stimuli in WD patients whereas other cytokines were comparable with controls; these immunol. alterations were not significantly different in patients with various disease activities. At the mucosal level, we found decreased CD4 T-cell percentage and a significantly impaired IFN-γ secretion. Conclusions: Our data define a defective cellular immune response in a large series of WD patients and point to an important pathogenetic role of impaired Th1 responses. The decreased monocyte IL-12 levels may result in reduced peripheral and mucosal IFN-γ production and lead to an increased susceptibility to T. whipplei infection in certain hosts.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

60
4 ov

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:707268 HCAPLUS
DOCUMENT NUMBER: 133:278661
TITLE: Primers, probes and antibodies for **diagnosis** of **Whipple disease**
INVENTOR(S): Raoult, Didier; La Scolla, Bernard; Birg, Marie-Laure; Fenollar, Florence
PATENT ASSIGNEE(S): Universite De La Mediterranee (Aix-Marseille

II), Fr.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058440	A1	20001005	WO 2000-FR754	20000324
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2791356	A1	20000929	FR 1999-3989	19990326
FR 2791357	A1	20000929	FR 1999-6679	19990521
FR 2791357	B1	20030516		
EP 1165750	A1	20020102	EP 2000-914252	20000324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539819	T2	20021126	JP 2000-608721	20000324

PRIORITY APPLN. INFO.:
FR 1999-3989 A 19990326
FR 1999-6679 A 19990521
WO 2000-FR754 W 20000324

AB The invention relates to a method for in **vitro** serol. **diagnosis** of **Whipple disease**, whereby the bacteria responsible for said disease is isolated and established in a culture and brought into contact with the serum of biol. fluid of a patient. The invention also relates to useful oligonucleotides with a probe and a primer for amplification, sequencing and **detection** of gene rpoB of **Tropheryma whippelii**.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1971:97072 HCAPLUS
DOCUMENT NUMBER: 74:97072
TITLE: Incorporation of L-leucine-14C into immunoglobulins by jejunal biopsies of patients with celiac sprue and other gastrointestinal diseases
AUTHOR(S): Loeb, P. M.; Strober, Warren; Falchuk, Z. M.; Laster, Leonard
CORPORATE SOURCE: Dig. Hered. Dis. Branch, Natl. Inst. Arthritis Metab. Dis., Bethesda, MD, USA
SOURCE: Journal of Clinical Investigation (1971), 50(3), 559-69
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Incorporation of L-leucine-14C into proteins and immunoglobulins in **vitro** was **determined** in jejunal biopsy specimens from normal volunteers, patients with celiac sprue before and after introduction of gluten into the diet, patients with **Whipple** 's **disease** in remission, and patients with immune deficiency states. One patient with celiac sprue and with normal intestinal histology had a normal value for incorporation into IgA; the other 4 patients with flat mucosas had elevated values. In **Whipple**'s **disease** in remission, values for incorporation into total protein and IgA were within the control limits, whereas incorporation into soluble protein was increased. Patients with hypogammaglobulinemia IgA deficiency had normal or elevated values for incorporation into total and soluble proteins; in these cases, however, no incorporation into IgA was **detected** . Biopsies from the four celiac sprue patients studied revealed that with introduction of gluten into the diet (a) incorporation into total protein, soluble protein, or both, increased; (b) incorporation into IgA increased in all patients, and in 2 instances the increase was greater than the increase in incorporation into total protein; and (c) incorporation into IgM increased in all patients. The changes during gluten administration usually occurred before changes in gastrointestinal absorptive function or in concentration of IgA in serum could be **detected.** These results indicate that gluten challenge stimulates increased local intestinal synthesis of immunoglobulins in patients with celiac sprue. The reaction occurs within days and it is possible that it plays a primary role in the pathogenesis of the disease.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:53:09 ON 13 NOV 2003)
L11 42 S L10
L12 25 DUP REM L11 (17 DUPLICATES REMOVED)

L12 ANSWER 1 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003420487 IN-PROCESS
DOCUMENT NUMBER: 22840818 PubMed ID: 12959718
TITLE: **Whipple**'s **disease.**
AUTHOR: Fenollar Florence; Raoult Didier
CORPORATE SOURCE: Unite des Rickettsies, CNRS UMR 6020, IFR 48, Faculte de medecine, Universite de la Mediterranee, 27 Boulevard Jean Moulin, 13385 Marseille cedex 05, France.
SOURCE: CURRENT GASTROENTEROLOGY REPORTS, (2003 Oct) 5 (5) 379-85.
Journal code: 100888896. ISSN: 1522-8037.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030909
Last Updated on STN: 20031001

AB **Whipple**'s **disease** is an infectious disease caused by a gram-positive bacterium, Tropheryma whipplei. The first case was reported in 1907 by GH Whipple. Its classic symptoms are diarrhea and arthralgias, but symptoms can be various. Cardiac or central nervous system involvement, not always associated with digestive symptoms, may also be observed. For a long time, **diagnosis** has been based on duodenal biopsy, which is

positive using periodic acid-Schiff staining. However, for patients without digestive symptoms, results can be negative, leading to a delay in **diagnosis**. For 10 years, a tool based on polymerase chain reaction targeting the 16S rDNA sequence has been used. In **vitro** culture of the bacterium, achieved 3 years ago, has allowed new perspectives for **diagnosis** and treatment. The natural evolution of the disease without treatment is always fatal. Current treatment is based on administration of trimethoprim-sulfamethoxazole for at least 1 year.

L12 ANSWER 2 OF 25 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003040366 MEDLINE
DOCUMENT NUMBER: 22436057 PubMed ID: 12547551
TITLE: **Whipple's disease**.
AUTHOR: Marth Thomas; Raoult Didier
CORPORATE SOURCE: Division of Gastroenterology, Stiftung Deutsche Klinik fur Diagnostik, Wiesbaden, Germany.. marth.gastro2@dkd-wiesbaden.de
SOURCE: LANCET, (2003 Jan 18) 361 (9353) 239-46. Ref: 116
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030128
Last Updated on STN: 20030206
Entered Medline: 20030205

AB **Whipple's disease**, or **intestinal lipodystrophy**, is a systemic infectious disorder affecting mostly middle-aged white men. Patients present with weight loss, arthralgia, diarrhoea, and abdominal pain. The disease is commonly **diagnosed** by small-bowel biopsy; the appearance of the sample is characterised by inclusions in the lamina propria staining with periodic-acid-Schiff, which represent the causative bacteria. Tropheryma whipplei has been classified as an actinomycete and has been propagated in **vitro**, which allows the possibility of improving **diagnostic** strategies, for example through antibody-based **detection** of the bacillus on duodenal tissue or in circulating monocytes. Cell-mediated immunity in active and inactive **Whipple's disease** has subtle defects that might predispose some individuals to symptomatic infection with this bacillus, which probably occurs ubiquitously. Although most patients respond well to empirical antibiotic treatment, some with relapsing disease have a poor outlook. The recent findings and concerted research might allow development of new strategies for **diagnosis**, treatment, and monitoring of patients with **Whipple's disease**.

L12 ANSWER 3 OF 25 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-140201 [13] WPIDS
DOC. NO. NON-CPI: N2003-111462
DOC. NO. CPI: C2003-035456
TITLE: Compositions for treating Th1/Th2 cell-related diseases comprise interleukin-2 or 4 and stromal cell-derived factor-1 alpha, their modulators,

modulators of tyrosine kinase Syk, ZAP-70 and nuclear factor of activated T cells.

DERWENT CLASS: B04 C06 D16 S03
INVENTOR(S): JINQUAN, T; POULSEN, L K
PATENT ASSIGNEE(S): (ALKA-N) ALK-ABELLO AS
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002089832	A2	20021114	(200313)*	EN	77
US 2003103938	A1	20030605	(200339)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002089832	A2	WO 2002-DK295	20020507
US 2003103938	A1 Provisional	US 2001-289711P	20010509
		US 2002-143528	20020509

PRIORITY APPLN. INFO: US 2001-289711P 20010509; DK 2001-726 20010509; US 2002-143528 20020509

AN 2003-140201 [13] WPIDS

AB WO 200289832 A UPAB: 20030224

NOVELTY - Compositions (C1) and (C2) comprising:

(a) Interleukin-4 (IL-4) (C1)/IL-2 (C2) and stromal cell-derived factor-1 alpha (SDF-1 alpha) (SF);

(b) IL-4 (C1)/IL-2 (C2) stimulant and stimulant of SF;

(c) Antagonist (Ant) of IL-2 (C1)/Ant of IL-4 (C2) and Ant of SF;

(d) Inhibitor (C1)/stimulant (C2) of Syk or NFAT1;

(e) Stimulant (C1)/inhibitor (C2) of ZAP-70 or NFAT2; or

(f) IL-4 (C1)/IL-2 (C2) stimulating adjuvant and SF, are new.

DETAILED DESCRIPTION - Compositions (C1) and (C2) comprise active substances selected from:

(a) Interleukin-4 (IL-4) (C1) or IL-2 (C2) and stromal cell-derived factor-1 alpha (SDF-1 alpha);

(b) IL-4 (C1) or IL-2 (C2) stimulant and stimulant of SDF-1 alpha ;

(c) Antagonist of IL-2 (C1) or antagonist of IL-4 (C2) and antagonist of SDF-1 alpha ;

(d) Inhibitor (C1) or stimulant (C2) of Syk or NFAT1;

(e) Stimulant (C1) or inhibitor (C2) of ZAP-70 or NFAT2;

(f) IL-4 (C1) or IL-2 (C2) stimulating adjuvant and SDF-1 alpha ;

(g) A functional derivative, analogue or part of any of the substances (a)-(f); or

(h) a combination of any of the substances relative to (C1) or (C2).

INDEPENDENT CLAIMS are also included for the following:

(1) an antisense peptide nucleic acid (APNA) that is complementary to a DNA molecule encoding the tyrosine kinase Syk or ZAP-70 or its part for preventing or treating a Th1/Th2 cell-related disease by modulating Th1/Th2 ratio;

(2) Evaluating (M1) the T helper cell profile comprising obtaining a T helper cell containing sample, measuring the level of phosphorylated Syk, phosphorylated ZAP-70, intranucleic NFAT1 and/or intranucleic NFAT2 and using the measuring results obtained to assess the Th1/Th2 level;

(3) Testing (M2) the effect of a product or a method on the Th1/Th2 ratio comprising obtaining a T helper cell containing culture with a known Th1/Th2 ratio, subjecting the T helper cells to the product or method, measuring the level of phosphorylated Syk, phosphorylated ZAP-70, intranucleic NFAT1 and/or intranucleic NFAT2 in the sample and using the measuring results obtained to assess the Th1/Th2 level;

(4) **Diagnostic** test kit comprising one or more probes specific for binding to phosphorylated Syk, phosphorylated ZAP-70, intranucleic NFAT1 and/or intranucleic NFAT2 and optionally a **detection** system; and

(5) Producing (M3) a culture enriched in Th1/Th2 cells by obtaining a T helper cell containing sample, subjecting the sample to an active substance as in (C1) and (C2) to modulate the Th1/Th2 ratio.

ACTIVITY - Immunosuppressive; Cytostatic; Antiallergic; Antipyretic; Antiasthmatic; Ophthalmological; Antiinflammatory; Antiulcer; Nephrotropic; Dermatological; Antirheumatic; Antiarthritic; Antidiabetic; Antithyroid; Cardiant.

No biological data available.

MECHANISM OF ACTION - Modulator of IL-4/IL-2, SDF-1 alpha , Syk, ZAP-70, NFAT1 or NFAT2 (all claimed); Antisense therapy.

Intracellular Th1 and Th2 cytokine was **detected** by flow cytometry. The CB T cells were stimulated with different combinations among interleukin-2 (IL-2) (10 ng/ml), IL-4 (10 ng/ml), and SDF-1 alpha (100 ng/ml), before intracellular cytokine assay. Th1 and Th2 cytokines assayed were interferon gamma (IFN- gamma), IL-4 or IFN- gamma and IL-4. The CD4+T cells from normal CB seem to be undifferentiated and unprimed showing naive Th pattern. In freshly isolated CB CD4+ T cells IFN- gamma and IL-4 double positive were 9.7%, whereas, IFN- gamma or IL-4 single positive were 8.5% or 12.1%, respectively. After 8 days of stimulation with IL-2 and SDF-1 alpha , the cells were switched to Th1 pattern in terms of expression of IFN- gamma (84%), whereas the stimulation with IL-4 an SDF-1 alpha lead the CBT cells to express Th2 pattern (90.3%). None of IL-2, IL-4 and SDF- alpha alone nor combination of IL-2 and IL-4 showed such function (data not shown). No significant difference was seen in terms of cellular proliferation between CB CD4+ T cells cultured without stimulus within 8 days as **detected** by (3H)thymidine incorporation into DNA assay. The cells cultured without stimulation had no significant change in terms of expression of intracellular cytokines during 8 days (data not shown). CXCR4 (CXC receptor 4) monoclonal antibody (mAb) significantly blocked such on-switch, whereas isotype Ig did not.

USE - (C1) and (C2) are useful for preventing or treating, respectively, a Th1/Th2 cell-related disease in a human or animal by reducing/increasing the Th1/Th2 ratio, respectively. (C1) and (C2) further comprise a pathogenic substance eliciting the

Th1/Th2-related disease to be treated. In (C1), the pathogenic substance is an infectious agent eliciting an infectious disease, or is an antigen, especially an autoantigen eliciting an autoimmune disease, or hapten or an allergen eliciting a delayed type hypersensitivity. In (C2) the pathogenic substance is a parasite organism or its portion, an antigen, preferably an allergen eliciting an allergic disease

Specifically, (C1) is useful for treating or preventing Th1 or Th2 cell-related diseases such as infectious disease, autoimmune disease, delayed type hypersensitivity, cancer, in a human or animal. (C2) is useful for treating or preventing a Th2 cell-related disease such as an allergic disease including hay fever, rhinoconjunctivitis, rhinitis and asthma, and also cancer.

(C1) and (C2) are either administered to the subject or T helper cells are removed from a subject and contacted ex vivo with the compositions.

Treatment may further comprise a second treatment involving the manipulation of the immune system such as vaccination, antigen specific immunotherapy, allergen specific immunotherapy, nonspecific immunotherapy or organ transplantation. APNA is useful in the manufacture of a medicament or for preventing or treating a Th1 or Th2 cell-related disease.

Cultures produced in (M3) are useful for in vitro or in vivo research and experiments (all claimed).

The autoimmune diseases treatable include encephalomyelopathic diseases, demyelinating and other autoimmune diseases such as multiple sclerosis, pneumonitis, sarcoidosis, ulcerative colitis, whipple's disease, vasculitis syndrome, Goodpastures syndrome, acute glomerulonephritis, gastrointestinal diseases such as Crohn's disease, skin diseases such as psoriasis, allergic skin disease, atopic dermatitis, joint diseases such as rheumatoid arthritis, musculoskeletal diseases such as myasthenia gravis, endocrine diseases such as insulin dependent diabetes mellitus, autoimmune thyroiditis, hyperthyroidism, cardiovascular diseases such as cardiomyopathy, vasculitis, cardiovascular disease associated with systemic diseases such as systemic lupus erythematosus, scleroderma, and polyarthritis nodosa.

Dwg.0/4

L12 ANSWER 4 OF 25 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER:	2003-328592 [31] WPIDS
DOC. NO. CPI:	C2003-111176
TITLE:	Treating an inflammatory disease, e.g. systemic lupus erythematosus, arthritis, hepatitis, dermatitis, systemic sclerosis, scleroderma, thyroiditis comprises administering a PRO301, PRO362 or PRO245 antagonist or its fragment.
DERWENT CLASS:	B04 D16
INVENTOR(S):	ASHKENAZI, A; FONG, S; GODDARD, A; GURNEY, A L; NAPIER, M A; TUMAS, D; WOOD, W I
PATENT ASSIGNEE(S):	(GETH) GENENTECH INC
COUNTRY COUNT:	1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002182206	A1	20021205	(200304)*		83

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002182206 A1	Provisional	US 1997-66364P	19971121
	Provisional	US 1998-78936P	19980320
	Cont of	WO 1998-US19437	19980917
	Cont of	WO 1998-US24855	19981120
	Cont of	US 1999-254465	19990305
		US 2001-953499	20010914

PRIORITY APPLN. INFO: US 2001-953499 20010914; US 1997-66364P 19971121; US 1998-78936P 19980320; WO 1998-US19437 19980917; WO 1998-US24855 19981120; US 1999-254465 19990305

AN 2003-328592 [31] WPIDS

AB US2002182206 A UPAB: 20030719

NOVELTY - Treating an inflammatory disease comprises administering a therapeutic amount of a PRO301, PRO362 or PRO245 antagonist or its fragment.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) **determining** the presence of PRO301, PRO362 or PRO245 polypeptide;

(2) **diagnosing** an inflammatory disease in a mammal;

(3) inhibiting growth of tumor cells;

(4) **diagnosing** tumor in a mammal;

(5) an isolated antibody that binds to the PRO301or PRO362 polypeptide;

(6) a composition comprising the antibody and a carrier;

(7) an isolated nucleic acid comprising: (a) a DNA having at least 95% sequence identity to a DNA molecule encoding a PRO301 polypeptide comprising the amino acids 28-235, 28-258 or 1-299 of a sequence of 299 amino acids, fully defined in the specification; (b) a DNA having at least 80% sequence identity to a DNA molecule encoding a PRO362 polypeptide comprising the amino acids 1-321 or 271-280 of a sequence of 321 amino acids, fully defined in the specification; (c) a DNA having at least 95% sequence identity to a DNA molecule encoding the same mature polypeptide encoded by the cDNA in ATCC Deposit Number 209432 (designation: DNA40628-1216), or its complement; or (d) a DNA having at least 80% sequence identity to a DNA molecule encoding the same mature polypeptide encoded by the cDNA in ATCC Deposit Number 209620 (designation: DNA45416-125 1), or its complement;

(8) producing PRO301, PRO362 or PRO245 polypeptides by culturing a host cell under conditions suitable for the expression of the polypeptides, and recovering the polypeptides from the cell culture; and

(9) isolated native sequences of PRO301 or PRO362 polypeptides as cited above.

ACTIVITY - Antiinflammatory; Immunosuppressive; Dermatological; Antirheumatic; Antiarthritic; Antianemic; Antithyroid; Thyromimetic; Antidiabetic; Nootropic; Neuroprotective; Virucide; Cytostatic; Hepatotropic.

The antiproliferative activity of the PRO301 and PRO362 polypeptides was **determined** in the investigational, disease-oriented in **vitro** anti-cancer drug discovery assay

using sulforhodamine B dye binding assay. 60 tumor cell lines were employed. Results showed at least 50% growth inhibitory effect at one or more concentrations.

MECHANISM OF ACTION - Gene therapy.

USE - The method is useful for treating an inflammatory disease, such as inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis, scleroderma, idiopathic inflammatory myopathies, dermatomyositis, polymyositis, Sjorgen's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, immune pancytopenia, paroxysmal nocturnal hemoglobinuria, autoimmune thrombocytopenia, idiopathic thrombocytopenia purpura, immune-mediated thrombocytopenia, thyroiditis, Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis, diabetes mellitus, immune-mediated renal disease, glomerulonephritis, tubulointerstitial nephritis, demyelinating diseases of the central and peripheral nervous systems, multiple sclerosis, idiopathic polyneuropathy, hepatobiliary diseases, infectious hepatitis such as hepatitis A, B, C, D, E and other nonhepatotropin viruses, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerosing cholangitis, inflammatory and firbrotic lung diseases (e.g. cystic fibrosis), gluten-sensitive enteropathy, **Whipple's disease**, autoimmune or immune-mediated skin diseases, bullous skin diseases, erythema multiforme, contact dermatitis, psoriasis, allergic diseases, eosinophilic pneumonia, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, or transplantation associated diseases including graft rejection and graft-versus host disease (all claimed).

Dwg.0/21

L12 ANSWER 5 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

ACCESSION NUMBER: 2003:34604 SCISEARCH

THE GENUINE ARTICLE: 625WG

TITLE: Emended description of Rickettsia felis (Bouyer et al. 2001), a temperature-dependent cultured bacterium

AUTHOR: La Scola B; Meconi S; Fenollar F; Rolain J M; Roux V; Raoult D (Reprint)

CORPORATE SOURCE: Univ Mediterranee, Fac Med, Unite Rickettsies, CNRS UPRESA 6020, 27 Bd Jean Moulin, F-13385 Marseille 05, France (Reprint); Univ Mediterranee, Fac Med, Unite Rickettsies, CNRS UPRESA 6020, F-13385 Marseille 05, France

COUNTRY OF AUTHOR: France

SOURCE: INTERNATIONAL JOURNAL OF SYSTEMATIC AND EVOLUTIONARY MICROBIOLOGY, (NOV 2002) Vol. 52, Part 6, pp. 2035-2041.
Publisher: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AG, BERKS, ENGLAND.
ISSN: 1466-5026.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB On the basis of phenotypic data obtained on the strain Marseille-URRWFXCaI2T, isolated from the cat flea Ctenocephalides

felis, the description of Rickettsia felis (Bouyer et al., 2001) is emended and Marseille-URRWFXCaI2T is proposed as the type strain of the species. On the basis of polyphasic characterization, especially the inability to grow at temperatures higher than 32 degreesC on Vero cells that allow growth of other Rickettsia to at least 35 degreesC, it is confirmed that this agent, although different from other recognized rickettsial species, is genotypically indistinguishable from bacteria previously **detected** within cat fleas and provisionally named ELB. Comparison of the phenotypic characteristics previously described for R. felis and those observed for the isolate in this study indicated some differences, although concurrent analysis of the two was not possible as no extant isolates of the first isolate of R. felis exist.

L12 ANSWER 6 OF 25 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002676165 MEDLINE
DOCUMENT NUMBER: 22291658 PubMed ID: 12404221
TITLE: Dysregulated peripheral and mucosal Th1/Th2 response in **Whipple's disease**.
AUTHOR: Marth Thomas; Kleen Nicole; Stallmach Andreas; Ring Sabine; Aziz Sheriff; Schmidt Carsten; Strober Warren; Zeitz Martin; Schneider Thomas
CORPORATE SOURCE: Internal Medicine II, University of the Saarland, Homburg/Saar, Germany.. marth.gastro2@dkd-wiesbaden.de
SOURCE: GASTROENTEROLOGY, (2002 Nov) 123 (5) 1468-77. Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021120
Last Updated on STN: 20021217
Entered Medline: 20021209

AB BACKGROUND & AIMS: An impaired monocyte function and impaired interferon (IFN)-gamma production has been suggested as a possible pathogenetic factor in **Whipple's disease** (WD) and as a cause for the delayed elimination of Tropheryma whipplei in some patients. METHODS: We studied, in a series of 20 WD patients with various degrees of disease activity, cellular immune functions. RESULTS: We found an increased in **vitro** production of interleukin (IL)-4 by peripheral mononuclear blood cells as **determined** by enzyme-linked immunosorbent assay, but reduced secretion of IFN-gamma and IL-2 as compared with age- and sex-matched controls. In addition, we observed a significantly reduced monocyte IL-12 production in response to various stimuli in WD patients whereas other cytokines were comparable with controls; these immunologic alterations were not significantly different in patients with various disease activities. At the mucosal level, we found decreased CD4 T-cell percentage and a significantly impaired IFN-gamma secretion. CONCLUSIONS: Our data define a defective cellular immune response in a large series of WD patients and point to an important pathogenetic role of impaired Th1 responses. The decreased monocyte IL-12 levels may result in reduced peripheral and mucosal IFN-gamma production and lead to an increased susceptibility to T. whipplei infection in certain hosts.

L12 ANSWER 7 OF 25 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-611706 [58] WPIDS
DOC. NO. CPI: C2000-183108
TITLE: Isolated, established culture of **Tropheryma whippelii**, useful for producing **diagnostic** and therapeutic agents for **Whipple disease**.
DERWENT CLASS: B04 D16
INVENTOR(S): BIRG, M; FENOLLAR, F; LA SCOLA, B; RAOULT, D; BIRG, M L; LA SCOLLA, B
PATENT ASSIGNEE(S): (UYAI-N) UNIV AIX-MARSEILLE II; (UYME-N) UNIV MERITERRANEE AIX MARSEILLE II; (RAOU-I) RAOULT D
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000058440	A1	20001005	(200058)*	FR	42
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
FR 2791356	A1	20000929	(200058)		
FR 2791357	A1	20000929	(200058)		
AU 2000035648	A	20001016	(200106)		
EP 1165750	A1	20020102	(200209)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002539819	W	20021126	(200307)		52

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000058440	A1	WO 2000-FR754	20000324
FR 2791356	A1	FR 1999-3989	19990326
FR 2791357	A1	FR 1999-6679	19990521
AU 2000035648	A	AU 2000-35648	20000324
EP 1165750	A1	EP 2000-914252	20000324
		WO 2000-FR754	20000324
JP 2002539819	W	JP 2000-608721	20000324
		WO 2000-FR754	20000324

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000035648	A	Based on	WO 2000058440
EP 1165750	A1	Based on	WO 2000058440
JP 2002539819	W	Based on	WO 2000058440

PRIORITY APPLN. INFO: FR 1999-6679 19990521; FR 1999-3989 19990326
AN 2000-611706 [58] WPIDS
AB WO 200058440 A UPAB: 20001114
NOVELTY - The bacterium **Tropheryma whippelii**,

the causative agent of **Whipple disease**, in isolated form and established in culture, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) antigens (Ag) from **T. whippelii**;

(2) antibody (Ab) specific for Ag or **T. whippelii**;

(3) serological in **vitro diagnosis** of **Whipple disease**;

(4) kits for carrying out the method of (3);

(5) total or partial sequences (I) of the rpoB gene of **T. whippelii**; and

(6) a method for **detecting** presence or absence of **T. whippelii** in a sample by formation of nucleic acid complex with a specific probe.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Oligonucleotides derived from **T. whippelii** DNA block transcription, translation or proliferation of the bacterium by hybridizing to nucleic acid.

USE - **T. whippelii**, its antigens (Ag) and antibodies specific for them are used for in **vitro diagnosis** of infection, specifically **Whipple disease**. Oligonucleotides derived from the rpoB gene of **T. whippelii** are used:

(i) as probes for **detecting** the bacterium by standard hybridization methods;

(ii) as a probe for polymerase-based synthesis of the rpoB gene;

(iii) as gene therapy probes, specifically for treating **Whipple disease**; and

(iv) for DNA sequencing.

Dwg.0/4

L12 ANSWER 8 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:469496 SCISEARCH
THE GENUINE ARTICLE: 325KM
TITLE: **Whipple's disease**: Is **Tropheryma whippelii** (Whipple's bacillus) foodborne?
AUTHOR: Smith J L (Reprint)
CORPORATE SOURCE: EASTERN REG RES CTR, USDA ARS, 600 E MERMAID LANE, WYNDMOOR, PA 19038 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF FOOD SAFETY, (JUN 2000) Vol. 20, No. 2, pp. 65-84.
Publisher: FOOD NUTRITION PRESS INC, 6527 MAIN ST, P O BOX 374, TRUMBULL, CT 06611.
ISSN: 0149-6085.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: English
REFERENCE COUNT: 83

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Whipple's disease** is a rare systemic disease with symptoms nominated by diarrhea, weight loss, arthralgia or arthritis and abdominal pain. **Whipple's disease** is limited to humans and the disease is caused by infection with the grampositive bacterium, **Tropheryma whippelii**.

PCR **determinations** suggest that **T. whippelii** is an environmental actinomycete but studies on the organism have been limited due to the inability to culture the organism in **vitro**. Most patients are male Caucasians older than 50 years of age living in North and South America, England, continental Europe and Australia. The cellular immune system appears to control **T. whippelii** and patients with cellular immune defects appear to be more susceptible to **Whipple's disease**. The disease affects the gastrointestinal tract, the central nervous system, cardiovascular system and musculoskeletal system; however, other organs also may be affected **Whipple's disease** can be treated with antibiotics effective against gram-positive bacteria but relapses are common. Untreated **Whipple's disease** is usually fatal. Although the mode of transmission of **T. whippelii** in humans is unclear, it possibly occurs through the fecal-oral route and food and/or water may be the source of the organism.

L12 ANSWER 9 OF 25 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-040346 [04] WPIDS
DOC. NO. CPI: C2000-010722
TITLE: **Detecting** antibiotic resistance in microorganisms by in situ characterization of probes.
DERWENT CLASS: B04 D16
INVENTOR(S): APFEL, H; HAAS, R; TREBESIUS, K
PATENT ASSIGNEE(S): (CREA-N) CREATOGEN BIOSCIENCES GMBH; (CREA-N) CREATOGEN AG
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19916610	A1	19991125	(200004)*		28
WO 9961660	A1	19991202	(200004)	GE	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9942658	A	19991213	(200020)		
BR 9910646	A	20010130	(200110)		
EP 1078104	A1	20010228	(200113)	GE	
R: AT BE CH DE DK ES FR GB IE IT LI NL SE					
JP 2002516665	W	20020611	(200253)		70
EP 1078104	B1	20021009	(200274)	GE	
R: AT BE CH DE DK ES FR GB IE IT LI NL SE					
DE 59903029	G	20021114	(200282)		
ES 2189459	T3	20030701	(200347)		
AU 763105	B	20030710	(200355)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19916610	A1	DE 1999-19916610	19990413

WO 9961660	A1	WO 1999-EP3527	19990521
AU 9942658	A	AU 1999-42658	19990521
BR 9910646	A	BR 1999-10646	19990521
		WO 1999-EP3527	19990521
EP 1078104	A1	EP 1999-938039	19990521
		WO 1999-EP3527	19990521
JP 2002516665	W	WO 1999-EP3527	19990521
		JP 2000-551040	19990521
EP 1078104	B1	EP 1999-938039	19990521
		WO 1999-EP3527	19990521
DE 59903029	G	DE 1999-503029	19990521
		EP 1999-938039	19990521
		WO 1999-EP3527	19990521
ES 2189459	T3	EP 1999-938039	19990521
AU 763105	B	AU 1999-42658	19990521

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9942658	A	Based on	WO 9961660
BR 9910646	A	Based on	WO 9961660
EP 1078104	A1	Based on	WO 9961660
JP 2002516665	W	Based on	WO 9961660
EP 1078104	B1	Based on	WO 9961660
DE 59903029	G	Based on	EP 1078104
		Based on	WO 9961660
ES 2189459	T3	Based on	EP 1078104
AU 763105	B	Previous Publ.	AU 9942658
		Based on	WO 9961660

PRIORITY APPLN. INFO: DE 1998-19823098 19980522
AN 2000-040346 [04] WPIDS
AB DE 19916610 A UPAB: 20000124
NOVELTY - **Detecting** antibiotic resistance in microorganisms by in situ characterization of a probe hybridizing with an antibiotic resistance associated nucleic acid in a microorganism is new.

DETAILED DESCRIPTION - A method to **detect** antibiotic resistance in microorganisms comprises the steps: preparing a microorganism containing test sample; contacting the sample with at least one hybridization probe, specific for an antibiotic resistance associated nucleic acid in the microorganism, under conditions specific for hybridization of the probe; evaluating the sample in situ through characterizing the appearance or failure of hybridization. INDEPENDENT CLAIMS are also included for: a reagent kit for typing microorganisms and/or antibiotic resistance in microorganisms through in situ hybridization; and oligonucleotides designated ClaR1, ClaR2, ClaR3, ClaWT, Hyp1-16S-753, 120b, Hyp1-16S-585 or Hyp1-16S-219 or that is at least 10 nucleotides in length and derived from these.

USE - The method is used to test slow growing and/or in **vitro** difficult or non cultivatable pathogens, e.g. Helicobacter pylori, Mycobacteria, Porphyromonas gigivalis, Propionibacterium acnes, Borrelia burgdorferi, Mycoplasma, Chlamydia, **Tropheryma whippelii**, Bartonella legionella, Norkardia and Actinomycetes. The sample can be prepared from human or animal tissue or body fluids. The method is used to

test samples that have no previous preparation for the microorganism in question. In particular the method is used to **detect** antibiotic resistance against in bacteria and protozoa.
Dwg.0/1

L12 ANSWER 10 OF 25 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999191207 MEDLINE
DOCUMENT NUMBER: 99191207 PubMed ID: 10091107
TITLE: **Detection** of **Tropheryma whippelii** DNA (**Whipple's disease**) in faeces.
AUTHOR: Gross M; Jung C; Zoller W G
CORPORATE SOURCE: Medizinische Poliklinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat Munchen, Germany.. mgross@pk-i.med.uni-muenchen.de
SOURCE: ITALIAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (1999 Jan-Feb) 31 (1) 70-2.
Journal code: 9711056. ISSN: 1125-8055.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 20000706
Entered Medline: 19990520

AB To date the **diagnosis** of **Whipple's disease** is based mainly on the histopathological analysis of duodenal biopsies since **Tropheryma whippelii** cannot be cultured in **vitro**. We investigated the possibility to **diagnose Whipple's disease** by **detection** of bacterial DNA in faces. Nested polymerase chain reaction with amplification of part of the 16S rRNA gene of this bacterium in DNA extracted from faeces of a patient with **Whipple's disease** was performed. Sequencing of the polymerase chain reaction product revealed the sequence of **Tropheryma whippelii**. We conclude that **Whipple's disease** will be able to be **diagnosed** non-invasively by DNA analysis from the faeces as soon as more specific sequences of this bacteria are known.

L12 ANSWER 11 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97253330 EMBASE
DOCUMENT NUMBER: 1997253330
TITLE: Defects of monocyte interleukin 12 production and humoral immunity in **Whipple's disease**.
AUTHOR: Marth T.; Neurath M.; Cuccherini B.A.; Strober W.
CORPORATE SOURCE: Dr. T. Marth, Department of Internal Medicine II, University of the Saarland, 66424 Homburg/Saar, Germany. intmar@med-rz.uni-sb.de
SOURCE: Gastroenterology, (1997) 113/2 (442-448).
Refs: 21
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology

026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background and Aims: **Whipple's disease** (WD) is a systemic infection in which the causative bacteria typically accumulate within macrophages. The aim of this study was to test whether this macrophage dysfunction is the cause or result of previously shown T-cell defects. Methods: In **vitro** production of interleukin (IL)-12, IL-10, tumor necrosis factor α, interferon gamma (IFN- γ), and transforming growth factor β (TGF-β) from purified monocytes and peripheral blood mononuclear cells, cytokine expression on duodenal biopsy specimens, and serum cytokine and immunoglobulin (Ig) levels were tested in 9 patients with WD. Results: Reduced monocyte IL-12 production and decreased IFN-γ secretion by peripheral blood mononuclear cells in **vitro** were found, as well as reduced immunohistological staining for IL-12 and IFN-γ, but no decrease in other cytokines in patients with WD. A similar but less severe defect in 2 relatives with WD argued for a genetic basis of this abnormality. Serum IgG2, an IFN-γ-dependent Ig subclass, and serum TGF-β levels were reduced in patients with WD. Conclusions: The described monocyte defects in WD may result in a secondary reduction of IFN-γ production and IgG2 serum levels. This provides a rationale for additive immunotherapy in patients with antibiotic-refractory WD.

L12 ANSWER 12 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1997:461769 BIOSIS
DOCUMENT NUMBER: PREV199799760972
TITLE: Nucleic acid technology and infectious diseases.
AUTHOR(S): Wong, S. Y.; Woo, C. Y.; Luk, W. K.; Yuen, K. Y. [Reprint author]
CORPORATE SOURCE: Dep. Microbiol., Univ. Hong Kong, Queen Mary Hosp., Pokfulam, Hong Kong
SOURCE: Hong Kong Medical Journal, (1997) Vol. 3, No. 2, pp. 179-185.
ISSN: 1024-2708.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Oct 1997
Last Updated on STN: 27 Oct 1997

AB The past decade has witnessed an explosion in the knowledge of microbial genetics, pathogenesis, and antimicrobial resistance as a result of advances in molecular technology. This has brought important breakthroughs in the management of patients with infectious diseases, as organisms that had previously been difficult to demonstrate in **vitro** can now be **detected** by molecular techniques such as the polymerase chain reaction. Not only is rapid **diagnosis** now possible, but old diseases of uncertain aetiology have been found to have an infective origin, for instance, **Whipple's disease**. Molecular technology has also contributed greatly to epidemiological studies of outbreaks, understanding antimicrobial resistance, developing new antimicrobial agents, the in **vitro** synthesis of immunomodulators, production of vaccines, and gene therapy. The

limitations of these latest technologies, however, need to be remembered so that they yield meaningful information for patient care.

L12 ANSWER 13 OF 25 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97283557 MEDLINE
DOCUMENT NUMBER: 97283557 PubMed ID: 9137662
TITLE: Impaired monocyte function in patients successfully treated for **Whipple's disease**.
AUTHOR: Bai J C; Sen L; Diez R; Niveloni S; Maurino E C; Estevez M E; Boerr L A
CORPORATE SOURCE: Small Bowel Section, Hospital Nacional de Gastroenterologia, Academia Nacional de Medicina, Buenos Aires, Argentina.
SOURCE: ACTA GASTROENTEROLOGICA LATINOAMERICANA, (1996) 26 (2) 85-9.
Journal code: 0261505. ISSN: 0300-9033.
PUB. COUNTRY: Argentina
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970630

AB Peripheral blood mononuclear cells (monocytes) from patients with **Whipple's disease** in long-term remission were tested for their ability to handle intracellular microorganisms. Phagocytosis and lysis of Candida tropicalis by monocytes of patients (n = 12) and controls (n = 8) were quantified after 30 min of incubation. Phagocytosis was similar in both groups but intracellular killing of Candida tropicalis was significatively lower in patients ($p < 0.001$). We concluded that our study showed an in **vitro** defect in the intracellular killing function of monocytes in subjects in remission many years after **diagnosis** of **Whipple's disease**. The defective function did not seem to be related to relapse or to the susceptibility to other infections.

L12 ANSWER 14 OF 25 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97059257 MEDLINE
DOCUMENT NUMBER: 97059257 PubMed ID: 8903578
TITLE: **Whipple's disease**.
AUTHOR: Marth T; Strober W
CORPORATE SOURCE: Mucosal Immunity Section, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA.
SOURCE: SEMINARS IN GASTROINTESTINAL DISEASE, (1996 Jan) 7 (1) 41-8. Ref: 42
Journal code: 9100391. ISSN: 1049-5118.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970226

AB **Whipple's disease** (WD) is a rare systemic disease caused by infection with the recently identified actinomycetes, **Tropheryma whippelii**. The disorder affects mostly middle-aged men, and the major clinical features are weight loss, arthropathy, and diarrhea; other symptoms, caused by systemic infection, are not infrequent. The **diagnosis** is usually established by duodenal biopsy, which shows the pathognomonic periodic acid Schiff-positive infiltrates in the lamina propria. In addition, RT-polymerase chain reaction of tissue specimens can be used to verify the presence of **T whippelii**. In most cases, patients can be successfully treated by prolonged administration of antimicrobials, such as trimethoprim-sulfamethoxazole. The unusual chronic-relapsing course of the disease, the predisposition of middle-aged, HLA-B27-positive men for WD, and other characteristics of the disease imply that host factors are involved in the etiopathogenesis of WD. Indeed, it has been shown that patients with WD have suppressed delayed-type hypersensitivity responses in vivo and decreased in **vitro** T-cell responses, eg, to phytohemagglutinin and concanavalin A. In addition, serum-suppressor factors and shifts in T-cell subpopulations have been found. Perhaps most importantly, WD macrophages have a decreased ability to degrade intracellular microorganisms and patients have reduced numbers of circulating cells expressing CD11b, a cell adhesion and complement receptor molecule on macrophages involved in the activation of intracellular killing of pathogens. Most of those immunologic alterations also occur in patients with longstanding clinical remission, suggesting that this subtle host-defense defect plays an important role in disease pathogenesis.

L12 ANSWER 15 OF 25 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 94326463 MEDLINE
DOCUMENT NUMBER: 94326463 PubMed ID: 7519533
TITLE: Persistent reduction of complement receptor 3 alpha-chain expressing mononuclear blood cells and transient inhibitory serum factors in **Whipple's disease**.
AUTHOR: Marth T; Roux M; von Herbay A; Meuer S C; Feurle G E
CORPORATE SOURCE: DRK-Krankenhaus Neuwied, University of Bonn, Heidelberg.
SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1994 Aug) 72 (2) 217-26.
Journal code: 0356637. ISSN: 0090-1229.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940914
Last Updated on STN: 19960129
Entered Medline: 19940902

AB Several small studies have indicated an impaired cell mediated immune response as a possible cause for the delayed elimination of the bacteria in **Whipple's disease**. A specific defect, however, has not been defined. We examined the expression

of cell surface molecules and mitogenic responses of peripheral blood mononuclear cells in 27 patients with **Whipple**'s **disease** at different disease stages by indirect immunofluorescence and by measurement of [3H]thymidine incorporation, respectively. E-rosette formation and cutaneous reaction to seven recall antigens were **determined**. Matched healthy donors served as controls. We found a significantly reduced number of cells expressing the complement receptor 3 alpha-chain (= CD11b) in all patients. In florid disease, the number of activated cells (in particular CD58 positive cells) was increased and CD4/CD8 ratios were diminished. Proliferation to phytohemagglutinin and to sheep red blood cells was reduced at all stages of the disease. Serum of control persons reversed this decreased responsiveness especially in patients with active disease. Skin reaction was hypoergic in all patients. **Determination** of CD58 positive cells increased in patients with active disease may be useful to define the activity of the disease and the duration necessary for treatment. Transient inhibiting serum activities may impair the CD2/CD58 interaction. The reduction of cells expressing CD11b, the decreased proliferation, and the cutaneous hypoergy indicate a persisting defect of cell mediated immunity in vivo and in **vitro**. These defects may contribute to the impaired ability of patients with **Whipple**'s **disease** to eliminate bacteria.

L12 ANSWER 16 OF 25 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 88208132 MEDLINE
DOCUMENT NUMBER: 88208132 PubMed ID: 2452591
TITLE: [Immunological profile of **Whipple**'s **disease** evolving over a period of 17 years]. Profil immunologique d'une maladie de Whipple evoluant depuis 17 ans.
AUTHOR: Gras C; Kaplanski S; Farnarier C; Bongrand P; Chapoy P; Aubry P
CORPORATE SOURCE: Service d'Hepato-Gastroenterologie, Hopital d'Instruction des Armees A. Laveran, Marseille.
SOURCE: ANNALES DE MEDECINE INTERNE, (1988) 139 (1) 24-8. Journal code: 0171744. ISSN: 0003-410X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19960129
Entered Medline: 19880609

AB This report describes an immunological study made on a 58 years old patient with a **Whipple disease diagnosed** in 1969 and treated with different antibiotics. All attempts to stop the antibiotherapy resulted in reappearance of clinical symptoms. Further, this patient suffered anguillulosis infection in 1954 and this persists despite thiabendazole therapy, as shown by periodical creeping lunear dermatitis (larva currens). Laboratory investigations displayed low IgM levels and lack of cutaneous reactivity to conventional antigenic challenge. In **vitro** studies on granulocyte and monocyte phagocytic activity did not display any clearcut deficiency. Finally, this patient displayed peripheral lymphopenia and decrease of the T4+ (CD4) lymphocyte

subpopulation. The proliferative response of lymphocytes to phytohemagglutinin stimulation (a cellular T-cell function) was drastically decreased in assays performed during the 16 month duration of patient's exploration. This proliferative defect seems to be due to increased PGE2 release (a 3-5 fold increase was demonstrated), resulting in inhibition of interleukin 2 (IL2) synthesis and activity. Further, patient's lymphocyte normally expressed IL2 receptor. When the B lymphocyte dependent humoral response was assayed, normal B lymphocyte differentiation into plasmocytes was found. However the pokeweed mitogen induced proliferative response of B lymphocyte displayed major decrease in four sequential tests. This might be due to a lack of B cell growth factor (BCGF) activity, since this interleukin involved in T lymphocyte, B lymphocyte cooperation was not found in supernatants of patient's cell. Further, interleukin 1 (involved in macrophage lymphocyte cooperation) was normally produced. In conclusion, no deficiency of in **vitro** phagocytose was demonstrated.(ABSTRACT TRUNCATED AT 250 WORDS)

L12 ANSWER 17 OF 25 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 83111214 MEDLINE
DOCUMENT NUMBER: 83111214 PubMed ID: 6822903
TITLE: Tissue content and metabolism of myo-inositol in normal and lipodystrophic gerbils.
AUTHOR: Chu S H; Geyer R P
CONTRACT NUMBER: HL-12399 (NHLBI)
SOURCE: JOURNAL OF NUTRITION, (1983 Feb) 113 (2) 293-303. Journal code: 0404243. ISSN: 0022-3166.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198303
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19970203
Entered Medline: 19830324

AB Experiments were conducted to evaluate the effect of diet and sex difference on the development of an **intestinal lipodystrophy** due to myo-inositol deficiency. Tissue contents of free and lipid-bound myo-inositol as well as the activities of L-myo-inositol-1-phosphate synthase (EC 5.5.1.4) and phosphatase (EC 3.1.3.25), and myo-inositol oxygenase (EC 1.13.99.1) were **determined** in male and female gerbils under various conditions. The enzyme study proved that the essentiality of dietary myo-inositol for this species was not due to the lack of such enzyme activity. The lower susceptibility of male gerbils to myo-inositol deficiency could be explained by the contribution of the biosynthesis of myo-inositol in the testis, as shown by a difference between intact and castrated animals. Although feeding coconut oil to the myo-inositol-deficient female gerbils produced greater myo-inositol depletion as well as more severe intestinal lesion than the feeding of safflower oil, the difference in myo-inositol status could be only in part responsible for different degrees of lipodystrophy. Additionally, neither dietary type of fat nor exogenous myo-inositol altered the activities of either hepatic or intestinal synthase and phosphatase, or kidney oxygenase. Thus, this study indicates that both sex and dietary factors might influence myo-inositol status to varying extents, but the

diet-induced change in tissue myo-inositol was not reflected by the enzyme activity as measured in **vitro**.

L12 ANSWER 18 OF 25 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 80091764 MEDLINE
DOCUMENT NUMBER: 80091764 PubMed ID: 93049
TITLE: HLA B27 and defects in the T-cell system in **Whipple's disease.**
AUTHOR: Feurle G E; Dorken B; Schopf E; Lenhard V
SOURCE: EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1979 Oct) 9 (5) 385-9.
Journal code: 0245331. ISSN: 0014-2972.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198003
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800324

AB The cellular immune system was tested in nine patients with **Whipples' disease**. Three patients had active disease, and six had been in remission for up to 10 years. Intradermal delayed hypersensitivity reactions to candidin, trichophytin, tuberculin and varidase, T-cell counts as **determined** by E-rosettes, allogeneic stimulation of lymphocytes in the mixed lymphocyte culture, and mitogenic activation of lymphocytes by concanavalin A, phytohaemagglutinin and by pokeweed mitogen, were tested in the patients and compared with control subjects. HLA typing was performed in all patients. The reaction to tuberculin and varidase, the T-cell counts and the activation of lymphocytes by concanavalin A were significantly reduced in patients with active disease and in patients during remission. The reaction to candidin and trichophytin was poor even in the controls. The mean results of the mixed lymphocyte culture, phytohaemagglutinin, and pokeweed mitogen activation tests were not significantly different from the controls. In patients with active disease the mixed lymphocyte culture reaction and the T-cell counts were less than in patients in remission. The results suggest a persistent defect of T-cells in patients with **Whipple's disease**, a defect that is more severe in patients with active disease. The finding of HLA B27 in four of thenine patients supports the hypothesis of primary rather than secondary impairment of the cellular immune system in **Whipple's disease**
.

L12 ANSWER 19 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 78121356 EMBASE
DOCUMENT NUMBER: 1978121356
TITLE: Etiopathogenetic studies in a patient with **Whipple's disease.**
AUTHOR: Tytgat G.N.; Hoogendijk J.L.; Agenant D.; Schellekens Th. P.
CORPORATE SOURCE: Dept. Med., Div. Gastroenterol., Wilhelmina Gasth., Amsterdam, Netherlands
SOURCE: Digestion, (1977) 15/4 (309-321).
CODEN: DIGEBW

COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 048 Gastroenterology
006 Internal Medicine
031 Arthritis and Rheumatism
037 Drug Literature Index
009 Surgery
005 General Pathology and Pathological Anatomy
LANGUAGE: English
AB A patient is presented with **Whipple's disease**. Before treatment, Haemophilis influenzae type e, sensitive to tetracycline was cultured from multiple small intestinal biopsies. This isolated micro-organism was structurally similar to the one observed in the tissue. All further culture experiments during and after treatment proved negative except for one biopsy from which a tetracycline-resistant H. influenzae type e mutant was isolated. The immunological disturbances, mainly characterized by cutaneous anergy, in the absence of major humoral or in **vitro** lymphocytic impairment, regressed during treatment together with clinical remission of the disease. These findings are considered in favour of the secondary nature of the immunological abnormalities.

L12 ANSWER 20 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 77204028 EMBASE
DOCUMENT NUMBER: 1977204028
TITLE: Seronegative arthritis.
AUTHOR: Jubb R.W.; Hazleman B.L.
CORPORATE SOURCE: Dept. Rheumatol., Addenbrooke's Hosp., Cambridge, United Kingdom
SOURCE: Update, (1976) 13/8 (775-790). CODEN: UPDTAP
DOCUMENT TYPE: Journal
FILE SEGMENT: 031 Arthritis and Rheumatism
033 Orthopedic Surgery
006 Internal Medicine
LANGUAGE: English
AB The seronegative spondylarthritides, i.e., ankylosing spondylitis, psoriatic arthritis, Reiter's disease, ulcerative colitis, Crohn's disease, **Whipple's disease** and Behcet's syndrome, have the following features in common: negative tests for rheumatoid factor, absence of rheumatoid nodules, inflammatory peripheral arthritis, radiological sacroiliitis, evidence of clinical overlap between members of the group, and tendency to familial aggregation.

L12 ANSWER 21 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 78007312 EMBASE
DOCUMENT NUMBER: 1978007312
TITLE: **Detection** by electron microscope of rod shaped organisms in synovial membrane from a patient with the arthritis of **Whipple's disease**.
AUTHOR: Hawkins C.F.; Farr M.; Morris C.J.; et al.
CORPORATE SOURCE: Rheumatism Res. Wing, Univ. Birmingham, Edgbaston, United Kingdom
SOURCE: Annals of the Rheumatic Diseases, (1976) 35/6

(502-509).
CODEN: ARDIAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 031 Arthritis and Rheumatism
005 General Pathology and Pathological Anatomy
006 Internal Medicine
004 Microbiology
LANGUAGE: English
AB In **Whipple's disease** arthritis often precedes gastrointestinal symptoms, sometimes by many years. The most commonly affected joints are the knees, ankles, and wrists, though occasionally the spine, proximal interphalangeal joints, metacarpophalangeal joints, and elbows are affected. Histologic studies of the synovial membrane have been carried out, but no electron microscope studies (EM) have been reported. In 1961 a characteristic rod shaped organism was described in the intestinal mucosa and since then numerous EM studies of the jejunum (reviewed by Maizel et al., 1970) have confirmed this. The present authors found rodshaped organisms identical to those present in the jejunal mucosa in the synovial membrane of a man of 59 with **Whipple's disease**. These organisms probably caused inflammatory changes which were reflected in an increase of the cellular content and the high enzyme levels (acid phosphatase and 5 nucleotidase) of the synovial fluid. Tetracycline was effective in controlling the bowel lesion but only had a temporary effect upon the arthritis. Erythromycin controlled both the bowel lesion and the arthritis.

L12 ANSWER 22 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 77051312 EMBASE
DOCUMENT NUMBER: 1977051312
TITLE: [**Whipple disease**. An immunologic and electron microscopy study].
MALADIE DE WHIPPLE. ETUDE ELECTRONIQUE ET IMMUNOLOGIQUE.
AUTHOR: Barbier P.; Balasse Ketelbant P.; Kennes B.; et al.
CORPORATE SOURCE: Serv. Gastroenterol., Hop. Univ. St Pierre, Bruxelles, Belgium
SOURCE: Archives Francaises des Maladies de l'Appareil Digestif, (1975) 64/8 (659-666).
CODEN: AMADBS
DOCUMENT TYPE: Journal
FILE SEGMENT: 048 Gastroenterology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
006 Internal Medicine
LANGUAGE: French
AB Although the infectious origin of **Whipple disease** is well documented, immunologic factors seem to be an important predisposing factor. In the present case, the following aspects of the disease are reported: clinical, biologic, bacteriologic (Corynebacterium anaerobium), microscopic and electronic pathology. The latter demonstrates bacterial structures in the intercellular spaces which are progressively destroyed. Immunologic study indicates only slightly abnormal status of the humoral immune response, contrasting with the deeply depressed cell mediated immune reactions. There is a negative candidin and streptokinase streptodornase (SKD) skin test. The in **vitro** lymphocyte

culture demonstrates a greatly reduced response to PHA and an abnormally low secretion of MIF (migration inhibitory factor) in response to SKD. There are very few IgA plasmocytes in the intestinal mucosa. After 1 yr therapy, the only improved test of cell mediated immunity is the MIF response. The significance of the immunologic disorders reported in the case presented (a woman of 74), is still unknown as far as the pathogenesis and clinical evaluation are concerned.

L12 ANSWER 23 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 77054681 EMBASE
DOCUMENT NUMBER: 1977054681
TITLE: [**Whipple's disease**: histochemical and electron microscopic study].
MALATTIA DI WHIPPLE: STUDIO ISTOCHIMICO ED ULTRASTRUTTURALE.
AUTHOR: Biagini G.; Bianchi F.B.; Laschi R.
CORPORATE SOURCE: Ist. Microsc. Elettron. Clin., Univ. Bologna, Italy
SOURCE: Pathologica, (1975) 67/973-974 (453-463).
CODEN: PATHAB
DOCUMENT TYPE: Journal
FILE SEGMENT: 048 Gastroenterology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
LANGUAGE: Italian
AB A case of **Whipple disease** is described in a man aged 43. Intestine and liver biopsies were performed before and after antibiotic treatment. Electron microscopic study confirmed the presence of bacteria in the level of the small intestine and in the liver. The various stages of intracellular digestion of the bacteria were documented. The morphologic and humoural findings are discussed.

L12 ANSWER 24 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 74012159 EMBASE
DOCUMENT NUMBER: 1974012159
TITLE: Protein synthesis by human intestinal mucosa: variations with diseases of the gut.
AUTHOR: Warshaw A.L.; Laster L.
CORPORATE SOURCE: Dig. Hered. Ds. Branch, Nat. Inst. Arthr. Metab. Dig. Dis., NIH, Bethesda, Md., United States
SOURCE: Journal of Surgical Research, (1973) 14/4 (285-293).
CODEN: JSGRA2
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
023 Nuclear Medicine
048 Gastroenterology
009 Surgery
LANGUAGE: English
AB Studies of protein synthesis by human intestinal mucosa were performed by **determining** the in **vitro** incorporation of L leucine U C14 into the total proteins of peroral mucosal biopsy specimens. The mean value for normal mucosa was 1483 dpm/mg/30 min ± 402. In mucosa from patients with sprue the mean value for mucosal protein synthesis was 3056, a significant elevation which might reflect abnormally high cell turnover in this

disease. In mucosa from patients with abetalipoproteinemia the mean value for protein synthesis was 535. This value, which is significantly lower than normal, may be related to diminished or absent synthesis of beta lipoproteins by the intestine in this disease. The mean value for mucosal protein synthesis among patients with treated **Whipple**'s **disease** in remission was normal. Measurement of protein synthesis by intestinal mucosa, obtained by peroral biopsy, appears to be useful in assessing metabolic aberrations and adaptations of the gut.

L12 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 67098047 MEDLINE
DOCUMENT NUMBER: 67098047 PubMed ID: 4163799
TITLE: Malacoplakia. Discussion of pathogenesis and report of three cases including one of fatal gastric and colonic involvement.
AUTHOR: Yunis E J; Estevez J M; Pinzon G J; Moran T J
SOURCE: ARCHIVES OF PATHOLOGY, (1967 Feb) 83 (2) 180-7. Journal code: 7605251. ISSN: 0363-0153.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 196704
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19670426

(FILE 'HCAPLUS' ENTERED AT 10:56:37 ON 13 NOV 2003)
L17 19 SEA FILE=HCAPLUS ABB=ON PLU=ON (WHIPPLE?(1W)(DISEAS? OR DISORDER) OR INTESTIN?(W)(LIPODYSTROPH? OR LIPO DYSTROPH?)) AND (TROPHERYM? OR T)(W)WHIPPEL?
L18 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN?)
L19 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND VITRO

L20 0 L19 NOT L10

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:58:14 ON 13 NOV 2003)
L21 13 S L19
L22 0 S L21 NOT L11

(FILE 'USPATFULL' ENTERED AT 10:59:36 ON 13 NOV 2003)
L23 8 SEA FILE=USPATFULL ABB=ON PLU=ON (WHIPPLE?(1W)(DISEAS? OR DISORDER) OR INTESTIN?(W)(LIPODYSTROPH? OR LIPO DYSTROPH?))(L)((TROPHERYM? OR T)(W)WHIPPEL?)

L23 ANSWER 1 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:266574 USPATFULL
TITLE: Secondary structure defining database and methods for determining identity and geographic origin of an unknown bioagent thereby
INVENTOR(S): Ecker, David J., Encinitas, CA, UNITED STATES
Griffey, Richard H., Vista, CA, UNITED STATES
Sampath, Rangarajan, San Diego, CA, UNITED STATES
Hofstadler, Steven, Oceanside, CA, UNITED STATES

McNeil, John, La Jolla, CA, UNITED STATES
Crooke, Stanley T., Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003187593	A1	20031002
APPLICATION INFO.:	US 2003-340482	A1	20030110 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-891793, filed on 26 Jun 2001, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: COZEN O'CONNOR, P.C., 1900 MARKET STREET, PHILADELPHIA, PA, 19103-3508
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 29 Drawing Page(s)
LINE COUNT: 1754
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the field of investigational bioinformatics and more particularly to secondary structure defining databases. The present invention further relates to methods for interrogating a database as a source of molecular masses of known bioagents for comparing against the molecular mass of an unknown or selected bioagent to determine either the identity of the selected bioagent, and/or to determine the origin of the selected bioagent. The identification of the bioagent is important for determining a proper course of treatment and/or irradiation of the bioagent in such cases as biological warfare. Furthermore, the determination of the geographic origin of a selected bioagent will facilitate the identification of potential criminal identity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 702/020.000
INCLS: 435/006.000; 435/091.200; 435/005.000
NCL NCLM: 702/020.000
NCLS: 435/006.000; 435/091.200; 435/005.000

L23 ANSWER 2 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:266569 USPATFULL
TITLE: Secondary structure defining database and methods for determining identity and geographic origin of an unknown bioagent thereby
INVENTOR(S): Ecker, David J., Encinitas, CA, UNITED STATES
Griffey, Richard, Vista, CA, UNITED STATES
Sampath, Rangarajan, San Diego, CA, UNITED STATES
Hofstadler, Steven A., Oceanside, CA, UNITED STATES
McNeil, John, La Jolla, CA, UNITED STATES
Crooke, Stanley T., Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003187588	A1	20031002
APPLICATION INFO.:	US 2003-340321	A1	20030110 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-891793, filed on 26 Jun 2001, PENDING
DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: COZEN O'CONNOR, P.C., 1900 MARKET STREET, PHILADELPHIA, PA, 19103-3508
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Page(s)
LINE COUNT: 1792
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to the field of investigational bioinformatics and more particularly to secondary structure defining databases. The present invention further relates to methods for interrogating a database as a source of molecular masses of known bioagents for comparing against the molecular mass of an unknown or selected bioagent to determine either the identity of the selected bioagent, and/or to determine the origin of the selected bioagent. The identification of the bioagent is important for determining a proper course of treatment and/or irradication of the bioagent in such cases as biological warfare. Furthermore, the determination of the geographic origin of a selected bioagent will facilitate the identification of potential criminal identity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 702/019.000
INCLS: 702/020.000; 435/005.000; 435/006.000
NCL NCLM: 702/019.000
NCLS: 702/020.000; 435/005.000; 435/006.000

L23 ANSWER 3 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:238975 USPATFULL
TITLE: Secondary structure defining database and methods for determining identity and geographic origin of an unknown bioagent thereby
INVENTOR(S): Ecker, David J., Encinitas, CA, UNITED STATES
Griffey, Richard H., Vista, CA, UNITED STATES
Sampath, Rangarajan, San Diego, CA, UNITED STATES
Hofstadler, Steven A., Oceanside, CA, UNITED STATES
McNeil, John, La Jolla, CA, UNITED STATES
Crooke, Stanley T., Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003167134	A1	20030904
APPLICATION INFO.:	US 2003-340483	A1	20030110 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-891793, filed on 26 Jun 2001, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Paul K. Legaard, COZEN O' CONNOR, 1900 Market Street, Philadelphia, PA, 19103
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Page(s)
LINE COUNT: 1769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to the field of investigational bioinformatics and more particularly to secondary

structure defining databases. The present invention further relates to methods for interrogating a database as a source of molecular masses of known bioagents for comparing against the molecular mass of an unknown or selected bioagent to determine either the identity of the selected bioagent, and/or to determine the origin of the selected bioagent. The identification of the bioagent is important for determining a proper course of treatment and/or irradication of the bioagent in such cases as biological warfare. Furthermore, the determination of the geographic origin of a selected bioagent will facilitate the identification of potential criminal identity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 702/020.000
INCLS: 435/006.000; 435/005.000
NCL NCLM: 702/020.000
NCLS: 435/006.000; 435/005.000

L23 ANSWER 4 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:238974 USPATFULL
TITLE: Secondary structure defining database and methods for determining identity and geographic origin of an unknown bioagent thereby
INVENTOR(S): Ecker, David J., Encinitas, CA, UNITED STATES
Griffey, Richard H., Vista, CA, UNITED STATES
Sampath, Rangarajan, San Diego, CA, UNITED STATES
Hofstadler, Steven A., Oceanside, CA, UNITED STATES
McNeil, John, La Jolla, CA, UNITED STATES
Crooke, Stanley T., Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003167133	A1	20030904
APPLICATION INFO.:	US 2003-340461	A1	20030110 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-891793, filed on 26 Jun 2001, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: COZEN O'CONNOR, P.C., 1900 MARKET STREET, PHILADELPHIA, PA, 19103-3508
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 29 Drawing Page(s)
LINE COUNT: 1774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to the field of investigational bioinformatics and more particularly to secondary structure defining databases. The present invention further relates to methods for interrogating a database as a source of molecular masses of known bioagents for comparing against the molecular mass of an unknown or selected bioagent to determine either the identity of the selected bioagent, and/or to determine the origin of the selected bioagent. The identification of the bioagent is important for determining a proper course of treatment and/or irradication of the bioagent in such cases as biological warfare. Furthermore, the determination of the geographic origin of a selected bioagent will facilitate the identification of

potential criminal identity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 702/020.000
INCLS: 435/006.000; 435/005.000
NCL NCLM: 702/020.000
NCLS: 435/006.000; 435/005.000

L23 ANSWER 5 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:180294 USPATFULL
TITLE: Use of interleukin-4 antagonists and compositions thereof
INVENTOR(S): Pluenneke, John D., Parkville, MO, UNITED STATES
PATENT ASSIGNEE(S): Immunex Corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003124121	A1	20030703
APPLICATION INFO.:	US 2002-324493	A1	20021219 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-847816, filed on 1 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-785934, filed on 15 Feb 2001, ABANDONED Continuation-in-part of Ser. No. US 2000-665343, filed on 19 Sep 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-579808, filed on 26 May 2000, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: IMMUNEX CORPORATION, LAW DEPARTMENT, 51 UNIVERSITY STREET, SEATTLE, WA, 98101
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 3505
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating medical conditions induced by interleukin-4 involve administering an IL-4 antagonist to a patient afflicted with such a condition. Suitable IL-4 antagonists include, but are not limited to, IL-4 receptors (such as a soluble human IL-4 receptor), antibodies that bind IL-4, antibodies that bind IL-4R, IL-4 muteins that bind to IL-4R but do not induce a biological response, molecules that inhibit IL-4-induced signal transduction, and other compounds that inhibit a biological effect that results from the binding of IL-4 to a cell surface IL-4R. Particular antibodies provided herein include human monoclonal antibodies generated by procedures involving immunization of transgenic mice. Such human antibodies may be raised against human IL-4 receptor. Certain of the antibodies inhibit both IL-4-induced and IL-13-induced biological activities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/143.100
INCLS: 530/388.220
NCL NCLM: 424/143.100
NCLS: 530/388.220

L23 ANSWER 6 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:120056 USPATFULL

TITLE: Secondary structure defining database and methods for determining identity and geographic origin of an unknown bioagent thereby

INVENTOR(S): Ecker, David J., Encinitas, CA, UNITED STATES
Griffey, Richard H., Vista, CA, UNITED STATES
Sampath, Rangarajan, San Diego, CA, UNITED STATES
Hofstadler, Steven A., Oceanside, CA, UNITED STATES
McNeil, John, La Jolla, CA, UNITED STATES
Crooke, Stanley T., Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003082539	A1	20030501	
APPLICATION INFO.:	US 2001-891793	A1	20010626	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Paul K. Legaard, WOODCOCK WASHBURN LLP, 46th Floor, One Liberty Place, Philadelphia, PA, 19103
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 29 Drawing Page(s)
LINE COUNT: 1686
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the field of investigational bioinformatics and more particularly to secondary structure defining databases. The present invention further relates to methods for interrogating a database as a source of molecular masses of known bioagents for comparing against the molecular mass of an unknown or selected bioagent to determine either the identity of the selected bioagent, and/or to determine the origin of the selected bioagent. The identification of the bioagent is important for determining a proper course of treatment and/or irradiation of the bioagent in such cases as biological warfare. Furthermore, the determination of the geographic origin of a selected bioagent will facilitate the identification of potential criminal identity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/005.000; 702/020.000
NCL NCLM: 435/006.000
NCLS: 435/005.000; 702/020.000

L23 ANSWER 7 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2002:136568 USPATFULL
TITLE: Methods to detect granulocytic ehrlichiosis
INVENTOR(S): Persing, David H., Rochester, MN, United States
Bruinsma, Elizabeth S., Rochester, MN, United States
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, Rochester, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6403093	B1	20020611	
APPLICATION INFO.:	US 1997-828199		19970321	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Smith, Lynette R. F.
ASSISTANT EXAMINER: Baskar, Padma
LEGAL REPRESENTATIVE: Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1661
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An isolated nucleic acid molecule associated with human granulocytic ehrlichiosis is provided. Also provided are methods to detect the presence of the nucleic acid molecule, and antibodies specific for the polypeptide encoded by the nucleic acid molecule, in a sample derived from a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/184.100
INCLS: 424/185.100; 424/190.100; 424/136.100; 424/191.100; 424/192.100; 424/234.100; 424/241.100; 530/300.000; 530/350.000; 530/380.000; 530/387.100; 530/388.400; 530/388.700; 530/827.000; 435/069.100; 435/069.300
NCL NCLM: 424/184.100
NCLS: 424/136.100; 424/185.100; 424/190.100; 424/191.100; 424/192.100; 424/234.100; 424/241.100; 435/069.100; 435/069.300; 530/300.000; 530/350.000; 530/380.000; 530/387.100; 530/388.400; 530/388.700; 530/827.000

L23 ANSWER 8 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2002:4153 USPATFULL
TITLE: Use of interleukin-4 antagonists and compositions thereof
INVENTOR(S): Pluenneke, John D., Seattle, WA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002002132	A1	20020103
APPLICATION INFO.:	US 2001-785934	A1	20010215 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-665343, filed on 19 Sep 2000, ABANDONED
Continuation-in-part of Ser. No. US 2000-579808, filed on 26 May 2000, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: IMMUNEX CORPORATION, LAW DEPARTMENT, 51 UNIVERSITY STREET, SEATTLE, WA, 98101
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2402
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating medical conditions induced by interleukin-4 involve administering an IL-4 antagonist to a patient afflicted with such a condition. Suitable IL-4 antagonists include, but are not limited to, IL-4 receptors (such as a soluble human IL-4 receptor), antibodies that bind IL-4, antibodies that bind IL-4R, IL-4 muteins that bind to IL-4R but do not induce a biological response, molecules that inhibit IL-4-induced signal transduction,

and other compounds that inhibit a biological effect that results from the binding of IL-4 to a cell surface IL-4R.

Particular antibodies provided herein include human monoclonal antibodies generated by procedures involving immunization of transgenic mice. Such human antibodies may be raised against human IL-4 receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/012.000
NCL NCLM: 514/012.000

(FILE 'MEDLINE' ENTERED AT 11:00:18 ON 13 NOV 2003)
L24 1191 SEA FILE=MEDLINE ABB=ON PLU=ON "WHIPPLE'S DISEASE"/CT
L25 316229 SEA FILE=MEDLINE ABB=ON PLU=ON "IN VITRO"/CT
L26 7 SEA FILE=MEDLINE ABB=ON PLU=ON L24 AND L25

L26 ANSWER 1 OF 7 MEDLINE on STN
AN 80091764 MEDLINE
TI HLA B27 and defects in the T-cell system in Whipple's disease.
AU Feurle G E; Dorken B; Schopf E; Lenhard V
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1979 Oct) 9 (5) 385-9.
Journal code: 0245331. ISSN: 0014-2972.
AB The cellular immune system was tested in nine patients with Whipples' disease. Three patients had active disease, and six had been in remission for up to 10 years. Intradermal delayed hypersensitivity reactions to candidin, trichophytin, tuberculin and varidase, T-cell counts as determined by E-rosettes, allogeneic stimulation of lymphocytes in the mixed lymphocyte culture, and mitogenic activation of lymphocytes by concanavalin A, phytohaemagglutinin and by pokeweed mitogen, were tested in the patients and compared with control subjects. HLA typing was performed in all patients. The reaction to tuberculin and varidase, the T-cell counts and the activation of lymphocytes by concanavalin A were significantly reduced in patients with active disease and in patients during remission. The reaction to candidin and trichophytin was poor even in the controls. The mean results of the mixed lymphocyte culture, phytohaemagglutinin, and pokeweed mitogen activation tests were not significantly different from the controls. In patients with active disease the mixed lymphocyte culture reaction and the T-cell counts were less than in patients in remission. The results suggest a persistent defect of T-cells in patients with Whipple's disease, a defect that is more severe in patients with active disease. The finding of HLA B27 in four of thenine patients supports the hypothesis of primary rather than secondary impairment of the cellular immune system in Whipple's disease.

L26 ANSWER 2 OF 7 MEDLINE on STN
AN 73171464 MEDLINE
TI Protein synthesis by human intestinal mucosa: variations with diseases of the gut.
AU Warshaw A L; Laster L
SO JOURNAL OF SURGICAL RESEARCH, (1973 Apr) 14 (4) 285-93.
Journal code: 0376340. ISSN: 0022-4804.

L26 ANSWER 3 OF 7 MEDLINE on STN
AN 67098047 MEDLINE

TI Malacoplakia. Discussion of pathogenesis and report of three cases including one of fatal gastric and colonic involvement.
AU Yunis E J; Estevez J M; Pinzon G J; Moran T J
SO ARCHIVES OF PATHOLOGY, (1967 Feb) 83 (2) 180-7.
Journal code: 7605251. ISSN: 0363-0153.

L26 ANSWER 4 OF 7 MEDLINE on STN
AN 66134431 MEDLINE
TI The histogenesis of Whipple's disease: a cytochemical, electron microscopic, and electron histochemical study.
AU Sobel H J
SO BULLETIN OF THE NEW YORK ACADEMY OF MEDICINE, (1966 Jun) 42 (6) 514-5.
Journal code: 7505398. ISSN: 0028-7091.

L26 ANSWER 5 OF 7 MEDLINE on STN
AN 66129800 MEDLINE
TI Use of polyethylene glycol and phenol red as unabsorbed indicators for intestinal absorption studies in man.
AU Schedl H P
SO GUT, (1966 Apr) 7 (2) 159-63.
Journal code: 2985108R. ISSN: 0017-5749.

L26 ANSWER 6 OF 7 MEDLINE on STN
AN 66072732 MEDLINE
TI Bacteria in Whipple's disease. 3. Studies in two patients of antibodies in serum and cutaneous hypersensitivity against some bacterial antigens.
AU Dybker R; Kok N
SO ACTA PATHOLOGICA ET MICROBIOLOGICA SCANDINAVICA, (1965) 64 (3) 373-80.
Journal code: 7508471. ISSN: 0365-5555.

L26 ANSWER 7 OF 7 MEDLINE on STN
AN 66049193 MEDLINE
TI [Histological peculiarities of the experimental disease induced in rabbits by inoculation of Corynebacterium anaerobium strains isolated from Whipple's disease].
Particularites histologiques de la maladie experimentale provoquee chez le lapin par inoculation de souches de Corynebacterium anaerobium, isolees de maladie de Whipple.
AU Levaditi J C; Prevot A R; Caroli J; Nazimoff O
SO ANNALES DE L INSTITUT PASTEUR, (1965 Jul) 109 (1) 144-7.
Journal code: 7512320. ISSN: 0020-2444.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 11:01:30 ON 13 NOV 2003)

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L27        2795 S "RAOULT D"?/AU
L28         245 S ("LASCOLA B"? OR "LA SCOLA B"?)/AU
L29          22 S "BIRG M"?/AU
L30          93 S "FENOLLAR F"?/AU
L31           1 S L27 AND L28 AND L29 AND L30
L32         289 S L27 AND (L28 OR L29 OR L30)
L33          23 S L28 AND (L29 OR L30)
L34           5 S L29 AND L30
L35         103 S (L32 OR L27 OR L28 OR L29 OR L30) AND L8
L36           8 S L35 AND VITRO
L37          32 S L31 OR L33 OR L34 OR L36
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Author (s)

Searcher : Shears 308-4994

L38 9 DUP REM L37 (23 DUPLICATES REMOVED)

L38 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003370466 MEDLINE
DOCUMENT NUMBER: 22786473 PubMed ID: 12904394
TITLE: Culture of Tropheryma whipplei from human samples: a 3-year experience (1999 to 2002).
AUTHOR: **Fenollar Florence; Birg Marie-Laure** ; Gauduchon Valerie; Raoult Didier
CORPORATE SOURCE: Unite des Rickettsies, CNRS UMR 6020, IFR 48, Faculte de Medecine, Universite de la Mediterranee, 13385 Marseille cedex 05, France.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (2003 Aug) 41 (8) 3816-22.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030808
Last Updated on STN: 20031024
Entered Medline: 20031023

AB The culture of Tropheryma whipplei, the bacterium responsible for Whipple's disease, has been established only recently. Our objective is to describe, based on our experience, the culture of T. whipplei in HEL cells detected by immunofluorescence staining. Over 3 years, we received 18 samples for T. whipplei culture from 15 patients with Whipple's disease. Ten duodenal biopsy specimens from 10 patients with digestive symptoms were available. Five cardiac valves and three blood samples from five patients with endocarditis were also available. We correlated the results of culture with the type of sample and the culture procedure. Seven isolates were obtained, and three were subsequently established for more than 4 passages. The mean delay for the primary detection was 30 days. The bacterium was isolated more frequently from sterile specimens (5 of 8) than from duodenal biopsy specimens (2 of 10), but the difference (P = 0.14) was not significant. Decontamination of digestive samples containing colistin, amphotericin B, and cephalotin or ciprofloxacin did not impair the isolation of T. whipplei. The use of vancomycin precludes the primary isolation (7 of 12 versus 0 of 6; P = 0.08) and the establishment of T. whipplei (3 of 12 versus 0 of 6; P = 0.5). Omitting samples cultured with vancomycin, the establishment of the strain was significantly higher when antibiotics were prescribed for no more than 7 days (3 of 4 versus 0 of 8; P = 0.03). Our results demonstrate that samples must be collected within 1 week of an antibiotic regimen's initiation for the successful establishment of the bacterium.

L38 ANSWER 2 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2003420487 IN-PROCESS
DOCUMENT NUMBER: 22840818 PubMed ID: 12959718
TITLE: **Whipple**'s **disease.**
AUTHOR: **Fenollar Florence; Raoult Didier**
CORPORATE SOURCE: Unite des Rickettsies, CNRS UMR 6020, IFR 48, Faculte de medecine, Universite de la Mediterranee, 27 Boulevard Jean Moulin, 13385 Marseille cedex 05, France.

SOURCE: CURRENT GASTROENTEROLOGY REPORTS, (2003 Oct) 5 (5) 379-85.
Journal code: 100888896. ISSN: 1522-8037.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030909
Last Updated on STN: 20031001

AB **Whipple's disease** is an infectious disease caused by a gram-positive bacterium, Tropheryma whipplei. The first case was reported in 1907 by GH Whipple. Its classic symptoms are diarrhea and arthralgias, but symptoms can be various. Cardiac or central nervous system involvement, not always associated with digestive symptoms, may also be observed. For a long time, diagnosis has been based on duodenal biopsy, which is positive using periodic acid-Schiff staining. However, for patients without digestive symptoms, results can be negative, leading to a delay in diagnosis. For 10 years, a tool based on polymerase chain reaction targeting the 16S rDNA sequence has been used. In **vitro** culture of the bacterium, achieved 3 years ago, has allowed new perspectives for diagnosis and treatment. The natural evolution of the disease without treatment is always fatal. Current treatment is based on administration of trimethoprim-sulfamethoxazole for at least 1 year.

L38 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003040366 MEDLINE
DOCUMENT NUMBER: 22436057 PubMed ID: 12547551
TITLE: **Whipple's disease.**
AUTHOR: Marth Thomas; **Raoult Didier**
CORPORATE SOURCE: Division of Gastroenterology, Stiftung Deutsche Klinik fur Diagnostik, Wiesbaden, Germany...
marth.gastro2@dkd-wiesbaden.de
SOURCE: LANCET, (2003 Jan 18) 361 (9353) 239-46. Ref: 116
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030128
Last Updated on STN: 20030206
Entered Medline: 20030205

AB **Whipple's disease**, or **intestinal lipodystrophy**, is a systemic infectious disorder affecting mostly middle-aged white men. Patients present with weight loss, arthralgia, diarrhoea, and abdominal pain. The disease is commonly diagnosed by small-bowel biopsy; the appearance of the sample is characterised by inclusions in the lamina propria staining with periodic-acid-Schiff, which represent the causative bacteria. Tropheryma whipplei has been classified as an actinomycete and has been propagated in **vitro**, which allows the possibility of improving diagnostic strategies, for example through antibody-based detection of the bacillus on duodenal tissue or in circulating monocytes. Cell-mediated immunity in active and inactive

Whipple's disease has subtle defects that might predispose some individuals to symptomatic infection with this bacillus, which probably occurs ubiquitously. Although most patients respond well to empirical antibiotic treatment, some with relapsing disease have a poor outlook. The recent findings and concerted research might allow development of new strategies for diagnosis, treatment, and monitoring of patients with **Whipple's disease.**

L38 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:12911 HCAPLUS
DOCUMENT NUMBER: 138:268116
TITLE: Emended description of Rickettsia felis (Bouyer et al. 2001), a temperature-dependent cultured bacterium
AUTHOR(S): **La Scola, Bernard;** Meconi, Sonia; **Fenollar, Florence;** Rolain, Jean-Marc; Roux, Veronique; Raoult, Didier
CORPORATE SOURCE: Unite des Rickettsies, CNRS UPRESA 6020, Faculte de Medecine, Universite de la Mediterranee, Marseille, 13385, Fr.
SOURCE: International Journal of Systematic and Evolutionary Microbiology (2002), 52(6), 2035-2041
CODEN: ISEMF5; ISSN: 1466-5026
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On the basis of phenotypic data obtained on the strain Marseille-URRWFXCal2T, isolated from the cat flea Ctenocephalides felis, the description of Rickettsia felis is emended and Marseille-URRWFXCal2T is proposed as the type strain of the species. On the basis of polyphasic characterization, especially the inability to grow at temps. higher than 32°C on Vero cells that allow growth of other Rickettsia to at least 35°C, it is confirmed that this agent, although different from other recognized rickettsial species, is genotypically indistinguishable from bacteria previously detected within cat fleas and provisionally named ELB. Comparison of the phenotypic characteristics previously described for R. felis and those observed for the isolate in this study indicated some differences, although concurrent anal. of the two was not possible as no extant isolates of the first isolate of R. felis exist.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:600603 HCAPLUS
DOCUMENT NUMBER: 135:329166
TITLE: Description of Tropheryma whipplei gen. nov., sp. nov., the Whipple's disease bacillus
AUTHOR(S): **La Scola, Bernard; Fenollar, Florence;** Fournier, Pierre-Edouard; Altwegg, Martin; Mallet, Marie-Noelle; Raoult, Didier
CORPORATE SOURCE: Unite des Rickettsies, Universite de la Mediterranee, Faculte de Medecine, CNRS UPRESA

6020, Marseille, 13385, Fr.
SOURCE: International Journal of Systematic and Evolutionary Microbiology (2001), 51(4), 1471-1479
CODEN: ISEMF5; ISSN: 1466-5026
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A detailed characterization was performed of the Whipple's disease bacillus, strain Twist-MarseilleT, isolated from the cardiac valve of a patient with Whipple's disease bacillus endocarditis. This strain was isolated and maintained on human embryonic lung fibroblast monolayers, but could not be cultivated in the absence of living eukaryotic cells. Two morphol. forms were observed, with differing staining properties; an intracellular form with intact and degenerating bacteria within vacuoles of infected cells and an extracellular form with masses of bacteria embedded in an extracellular matrix. Determination of the DNA G+C content confirmed that it belongs to the high-G+C Gram-pos. bacteria. Strain Twist-MarseilleT (= CNCM 1-2202T) is proposed as the type strain of a new species within a new genus, Tropheryma whipplei gen. nov., sp. nov., that was provisionally created solely on the basis of 16S rRNA gene sequence data.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2001:155672 HCAPLUS
DOCUMENT NUMBER: 134:337971
TITLE: A flea-associated Rickettsia pathogenic for humans
AUTHOR(S): Raoult, Didier; **La Scola, Bernard;** Enea, Maryse; Fournier, Pierre-Edouard; Roux, Veronique; **Fenollar, Florence;** Galvao, Marcio A. M.; De Lamballerie, Xavier
CORPORATE SOURCE: Unite des Rickettsies, Marseille, 6020, Fr.
SOURCE: Emerging Infectious Diseases (2001), 7(1), 73-81
CODEN: EIDIFA; ISSN: 1080-6040
PUBLISHER: National Center for Infectious Diseases, Centers for Disease Control and Prevention
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rickettsia named the ELB agent, or "Rickettsia felis," was identified by mol. biol. techniques in American fleas in 1990 and later in four patients from Texas and Mexico. We attempted to isolate this rickettsia from infected fleas at various temps. and conditions. A representative isolate of the ELB agent, the Marseille strain, was characterized and used to develop a microimmunofluorescence test that detected reactive antibodies in human sera. The ELB agent was isolated from 19 of 20 groups of polymerase chain reaction-proven infected fleas. The microimmunofluorescence results provided serol. evidence of infection by the ELB agent in four patients with fever and rash in France (2) and Brazil (2), supporting the pathogenic role of this rickettsia. Our successful isolation of this rickettsia makes it available for use in serol. tests to determine its clin. spectrum, prevalence, and distribution.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2000:707268 HCAPLUS
DOCUMENT NUMBER: 133:278661
TITLE: Primers, probes and antibodies for diagnosis of **Whipple disease**
INVENTOR(S): **Raoult, Didier**; La Scolla, Bernard; **Birg, Marie-Laure**; **Fenollar, Florence**
PATENT ASSIGNEE(S): Universite De La Mediterranee (Aix-Marseille II), Fr.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058440	A1	20001005	WO 2000-FR754	20000324
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2791356	A1	20000929	FR 1999-3989	19990326
FR 2791357	A1	20000929	FR 1999-6679	19990521
FR 2791357	B1	20030516		
EP 1165750	A1	20020102	EP 2000-914252	20000324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539819	T2	20021126	JP 2000-608721	20000324

PRIORITY APPLN. INFO.:
FR 1999-3989 A 19990326
FR 1999-6679 A 19990521
WO 2000-FR754 W 20000324

AB The invention relates to a method for in **vitro** serol. diagnosis of **Whipple disease**, whereby the bacteria responsible for said disease is isolated and established in a culture and brought into contact with the serum of biol. fluid of a patient. The invention also relates to useful oligonucleotides with a probe and a primer for amplification, sequencing and detection of gene rpoB of **Tropheryma whippelii**.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000143076 MEDLINE
DOCUMENT NUMBER: 20143076 PubMed ID: 10699161
TITLE: Cultivation of the bacillus of Whipple's disease.

COMMENT: Comment in: N Engl J Med. 2000 Mar 2;342(9):648-50
Erratum in: N Engl J Med 2000 May 18;342(20):1538

AUTHOR: Raoult D; **Birg M L; La Scola B;**
Fournier P E; Enea M; Lepidi H; Roux V; Piette J C;
Vandenesch F; Vital-Durand D; Marrie T J
CORPORATE SOURCE: Unite des Rickettsies, Universite de la Mediterranee, Faculte de Medecine, Marseilles, France..
didier.raoult@medecine.univ-mrs.fr

SOURCE: NEW ENGLAND JOURNAL OF MEDICINE, (2000 Mar 2) 342 (9) 620-5.
Journal code: 0255562. ISSN: 0028-4793.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000613
Entered Medline: 20000302

AB BACKGROUND: Whipple's disease is a systemic bacterial infection, but to date no isolate of the bacterium has been established in subculture, and no strain of this bacterium has been available for study. METHODS: Using specimens from the aortic [corrected] valve of a patient with endocarditis due to Whipple's disease, we isolated and propagated a bacterium by inoculation in a human fibroblast cell line (HEL) with the use of a shell-vial assay. We tested serum samples from our patient, other patients with Whipple's disease, and control subjects for the presence of antibodies to this bacterium. RESULTS: The bacterium of Whipple's disease was grown successfully in HEL cells, and we established subcultures of the isolate. Indirect immunofluorescence assays showed that the patient's serum reacted specifically against the bacterium. Seven of 9 serum samples from patients with Whipple's disease had IgM antibody titers of 1:50 or more, as compared with 3 of 40 samples from the control subjects ($P<0.001$). Polyclonal antibodies against the bacterium were generated by inoculation of the microorganism into mice and were used to detect bacteria in the excised cardiac tissue from our patient on immunohistochemical analysis. The 16S ribosomal RNA gene of the cultured bacterium was identical to the sequence for Tropheryma whippelii identified previously in tissue samples from patients with Whipple's disease. The strain we have grown is available in the French National Collection. CONCLUSIONS: We cultivated the bacterium of Whipple's disease, detected specific antibodies in tissue from the source patient, and generated specific antibodies in mice to be used in the immunodetection of the microorganism in tissues. The development of a serologic test for Whipple's disease may now be possible.

L38 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999454878 MEDLINE
DOCUMENT NUMBER: 99454878 PubMed ID: 10523584
TITLE: Isolation of Rickettsia prowazekii from blood by shell vial cell culture.

AUTHOR: **Birg M L; La Scola B;** Roux V;
Brouqui P; Raoult D
CORPORATE SOURCE: Unite des Rickettsies, CNRS UPRESA 6020, Faculte de Medecine, 13385 Marseille Cedex 05, France.

SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1999 Nov) 37 (11)

3722-4.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991130

AB A blood sample from a patient who returned from Algeria with a fever inoculated on human embryonic lung fibroblasts by the shell vial cell culture technique led to the recovery of Rickettsia prowazekii. The last clinical strain was isolated 30 years ago. Shell vial cell culture is a versatile method that could replace the classic animal and/or embryonated egg inoculation.

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